

Sequence Listing

<110> Henry B. Lowman, Leonard G. Presta, Paula M. Jardieu, John Lowe

5 <120> Anti-IgE Antibodies and Method of Improving Polypeptides

<130> P1123R1

<140> US 09/109,207

10 <141> 1998-06-30

<150> US 60/051,554

<151> 1997-07-03

15 <160> 44

<210> 1

<211> 6127

<212> DNA

20 <213> Artificial

<220>

<221> Artificial

<222> 1-6127

25 <223> Expression plasmid

<400> 1

gaattcaact tctccatact ttggataagg aaatacagac atgaaaaatc 50

30 tcattgctga gttgttattt aagcttgccc aaaaagaaga agagtcgaat 100

gaactgtgtg cgcaggtaga agctttggag attatcgtca ctgcaatgct 150

35 tcgcaatatg gcgcaaaatg accaacagcg gttgattgat caggtagagg 200

gggcgctgta cgaggtaaag cccgatgcca gcattcctga cgacgatacg 250

gagctgctgc gcgattacgt aaagaagtta ttgaagcatc ctcgtcagta 300

40 aaaagttaat cttttcaaca gctgtcataa agttgtcacg gccgagactt 350

atagtcgctt tgtttttatt ttttaatgta tttgtaacta gaattcgagc 400

45 tcggtacccg gggatcctct cgaggttgag gtgattttat gaaaaagaat 450

atcgcatctt ttcttgcac tatgttcgtt ttttctattg ctacaaacgc 500

gtacgctgat atccagctga cccagtcccc gagctccttg tccgcctctg 550

50 tgggcgatag ggtcaccatc acctgccgtg ccagtcagag cgtcgattac 600

gaaggtgata gctacctgaa ctggtatcaa cagaaaccag gaaaagctcc 650

55 gaaactactg atttacgcgg cctcgtaact ggagtctgga gtcccttctc 700

gcttctctgg atccggttct gggacggatt tcaactctgac catcagcagt 750

ctgcagccag aagacttcgc aacttattac tgtcagcaaa gtcacgagga 800

60 tccgtacaca tttggacagg gtaccaaggt ggagatcaaa cgaactgtgg 850

ctgcaccatc tgtcttcac ttcccgcac ctgatgagca gttgaaatct 900

<220>

<221> Artificial

<222> 1-121

5 <223> F(ab) sequence derived from MAE11

<400> 3

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
1 5 10 15

10 Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
20 25 30

15 Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
35 40 45

Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
50 55 60

20 Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser
65 70 75

Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
80 85 90

25 Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
95 100 105

30 Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
110 115 120

Ser

35 <210> 4

<211> 121

<212> PRT

<213> Homo sapiens

40 <220>

<221> unsure

<222> 30, 104-108

<223> unknown amino acid

45 <400> 4

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
1 5 10 15

50 Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Xaa
20 25 30

Ser Asp Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly
35 40 45

55 Leu Glu Trp Val Ala Val Ile Ser Asn Gly Ser Asp Thr Tyr Tyr
50 55 60

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser
65 70 75

60 Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
80 85 90

Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Arg Phe Phe Xaa Xaa
 95 100 105

5 Xaa Xaa Xaa Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
 110 115 120

Ser

10 <210> 5
 <211> 111
 <212> PRT
 <213> Mus musculus

15 <400> 5
 Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu
 1 5 10 15

20 Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp
 20 25 30

 Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 35 40 45

25 Gln Pro Pro Ile Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Gly Ser
 50 55 60

30 Glu Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 65 70 75

 Thr Leu Asn Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Phe
 80 85 90

35 Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Ala Gly
 95 100 105

 Thr Lys Leu Glu Ile Lys
 110

40 <210> 6
 <211> 111
 <212> PRT
 <213> Artificial

45 <220>
 <221> Artificial
 <222> 1-111
 <223> F(ab) light chain sequence derived from MAE11

50 <400> 6
 Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
 1 5 10 15

55 Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Asp
 20 25 30

 Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 35 40 45

60 Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
 50 55 60

<221> Artificial
 <222> 1-114
 <223> Light chain sequence derived from MAE11

5 <400> 10
 Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
 1 5 10 15
 Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Asp
 10 20 25 30
 Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 35 40 45
 15 Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
 50 55 60
 Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 65 70 75
 20 Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
 80 85 90
 Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
 25 95 100 105
 Thr Lys Val Glu Ile Lys Arg Thr Val
 110

<210> 11
 <211> 114
 <212> PRT
 <213> Artificial

<220>
 <221> Artificial
 <222> 1-114
 <223> Heavy chain sequence derived from MAE11

40 <400> 11
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
 1 5 10 15
 Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
 45 20 25 30
 Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
 35 40 45
 50 Leu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr
 50 55 60
 Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
 65 70 75
 55 Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
 80 85 90
 Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
 60 95 100 105
 Trp His Phe Ala Val Trp Gly Gln Gly

5 <210> 12
 <211> 114
 <212> PRT
 <213> Artificial

10 <220>
 <221> Artificial
 <222> 1-114
 <223> Heavy chain sequence derived from MAE11

15 <400> 12
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
 1 5 10 15
 Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
 20 25 30
 Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
 35 40 45
 Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
 50 55 60
 Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
 65 70 75
 Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
 80 85 90
 Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
 95 100 105
 35 Trp His Phe Ala Val Trp Gly Gln Gly
 110

40 <210> 13
 <211> 218
 <212> PRT
 <213> Artificial

45 <220>
 <221> Artificial
 <222> 1-218
 <223> Light chain sequence derived from MAE11

50 <400> 13
 Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
 1 5 10 15
 Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Asp
 20 25 30
 Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 35 40 45
 Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
 50 55 60
 60 Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 65 70 75

	Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser	110	115	120
5	Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser	125	130	135
	Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val	140	145	150
10	Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly	155	160	165
	Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser	170	175	180
15	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser	185	190	195
20	Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro	200	205	210
	Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp	215	220	225
25	Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly	230	235	240
	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu	245	250	255
30	Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val	260	265	270
	Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly	275	280	285
35	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr	290	295	300
40	Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln	305	310	315
	Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys	320	325	330
45	Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly	335	340	345
50	Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu	350	355	360
	Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly	365	370	375
55	Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln	380	385	390
60	Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp	395	400	405
	Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg			

420

5

10

15 <213> Artificial

20 <223> Light chain sequence derived from MAE11

25

30

35

40

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55

60

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr

200

205

210

Lys Ser Phe Asn Arg Gly Glu Cys
215

5

<210> 16
<211> 451
<212> PRT
<213> Artificial

10

<220>
<221> Artificial
<222> 1-451
<223> Heavy chain sequence derived from MAE11

15

<400> 16
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
1 5 10 15

20

Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
20 25 30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
35 40 45

25

Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
50 55 60

30

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
65 70 75

Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
80 85 90

35

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
95 100 105

Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
110 115 120

40

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
125 130 135

45

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
140 145 150

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
155 160 165

50

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
170 175 180

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
185 190 195

55

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
200 205 210

60

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
215 220 225

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly

	20	25	30
	Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly		
	35	40	45
5	Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser		
	50	55	60
10	Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe		
	65	70	75
	Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr		
	80	85	90
15	Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly		
	95	100	105
	Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe		
	110	115	120
20	Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser		
	125	130	135
25	Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val		
	140	145	150
	Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu		
	155	160	165
30	Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser		
	170	175	180
	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val		
	185	190	195
35	Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr		
	200	205	210
40	Lys Ser Phe Asn Arg Gly Glu Cys		
	215		
	<210> 18		
	<211> 451		
	<212> PRT		
45	<213> Artificial		
	<220>		
	<221> Artificial		
	<222> 1-451		
50	<223> Heavy chain sequence derived from MAE11		
	<400> 18		
	Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly		
	1	5	10
55	Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr		
	20	25	30
60	Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly		
	35	40	45
	Leu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr		

00245035 144700

	50	55	60
	Asn Pro Ser Val Lys Gly Arg Ile Thr	Ile Ser Arg Asp Asp Ser	
	65	70	75
5	Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp		
	80	85	90
10	Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His		
	95	100	105
	Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser		
	110	115	120
15	Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser		
	125	130	135
	Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val		
	140	145	150
20	Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly		
	155	160	165
25	Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser		
	170	175	180
	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser		
	185	190	195
30	Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro		
	200	205	210
	Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp		
	215	220	225
35	Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly		
	230	235	240
40	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu		
	245	250	255
	Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val		
	260	265	270
45	Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly		
	275	280	285
	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr		
	290	295	300
50	Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln		
	305	310	315
55	Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		
	320	325	330
	Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly		
	335	340	345
60	Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu		
	350	355	360

Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
155 160 165

5 Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
170 175 180

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
185 190 195

10 Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
200 205 210

Lys Ser Phe Asn Arg Gly Glu Cys
215

15 <210> 20
<211> 229
<212> PRT
<213> Artificial

20 <220>
<221> Artificial
<222> 1-229
<223> Heavy chain F(ab) sequence derived from MAE11

25 <400> 20
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
1 5 10 15

30 Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
20 25 30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
35 35 40 45

Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
50 55 60

40 Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
65 70 75

Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
80 85 90

45 Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
95 100 105

Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
110 115 120

50 Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
125 130 135

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
140 145 150

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
155 160 165

60 Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
170 175 180

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
 200 205 210

5 Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 215 220 225

Lys Thr His Thr

10 <210> 22
 <211> 248
 <212> PRT
 <213> Artificial

15 <220>
 <221> Artificial
 <222> 1-248
 <223> sFv sequence derived from MAE11

20 <400> 22
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
 1 5 10 15

25 Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
 20 25 30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
 35 40 45

30 Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
 50 55 60

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
 65 70 75

35 Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
 80 85 90

40 Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
 95 100 105

Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
 110 115 120

45 Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly
 125 130 135

Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
 140 145 150

50 Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val
 155 160 165

55 Asp Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
 170 175 180

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu
 185 190 195

60 Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
 200 205 210

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
 215 220 225

5 Tyr Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln
 230 235 240

Gly Thr Lys Val Glu Ile Lys Arg
 245

10 <210> 23
 <211> 248
 <212> PRT
 <213> Artificial

15 <220>
 <221> Artificial
 <222> 1-248
 <223> sFv sequence derived from MAE11

20 <400> 23
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
 1 5 10 15

25 Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
 20 25 30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
 35 40 45

30 Leu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr
 50 55 60

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
 65 70 75

35 Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
 80 85 90

40 Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
 95 100 105

Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
 110 115 120

45 Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly
 125 130 135

Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
 140 145 150

50 Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val
 155 160 165

55 Asp Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
 170 175 180

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu
 185 190 195

60 Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
 200 205 210

5 Tyr Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln
230 235 240

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10      <210> 24
        <211> 218
        <212> PRT
        <213> Artificial
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15  <220>
    <221> Artificial
    <222> 1-218
    <223> Light chain F(ab)'2 sequence derived from MAE11

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20      <400> 24
      Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
        1               5               10              15

```

25 Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val Asp
20 25 30

Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
35 40 45

[illegible]

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
65 70 75

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
80 85 90

40 Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
95 100 105

Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
110 115 120

45 Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser
125 130 135

Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala	Lys	Val
				140					145					150

Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
155 160 165

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
55 170 175 180

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
185 190 195

60 Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
200 205 210

Lys Ser Phe Asn Arg Gly Glu Cys
215

5 <210> 25
<211> 233
<212> PRT
<213> Artificial

10 <220>
<221> Artificial sequence
<222> 1-233
<223> Heavy chain F(ab)'2 sequence derived from MAE11

15 <400> 25
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
1 5 10 15

Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
20 20 25 30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
35 40 45

25 Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
50 55 60

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
65 70 75

30 Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
80 85 90

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
95 100 105

35 Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
110 115 120

40 Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
125 130 135

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
140 145 150

45 Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
155 160 165

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
170 175 180

50 Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
185 190 195

55 Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
200 205 210

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
215 220 225

60 Lys Thr His Thr Cys Pro Pro Cys
230

<210> 26
 <211> 233
 <212> PRT
 <213> Artificial

5

<220>
 <221> Artificial
 <222> 1-233
 <223> Heavy chain F(ab)'2 sequence derived from MAE11

10

<400> 26
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
 1 5 10 15

15

Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
 20 25 30

20

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
 35 40 45

Leu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr
 50 55 60

25

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
 65 70 75

Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
 80 85 90

30

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
 95 100 105

Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
 110 115 120

35

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
 125 130 135

40

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
 140 145 150

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
 155 160 165

45

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
 170 175 180

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
 185 190 195

50

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
 200 205 210

55

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 215 220 225

Lys Thr His Thr Cys Pro Pro Cys
 230

60

<210> 27
 <211> 45
 <212> DNA

<213> Artificial
 <220>
 <221> Artificial
 5 <222> 1-45
 <223> Stop-Template Oligos for First-Round Mutagenesis
 <400> 27
 10 acctgccgtg ccagttaata agtctaataa gaaggtgata gctac 45
 <210> 28
 <211> 46
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